

**INTERNATIONAL SEARCH REPORT**

International Application No  
PCT/EP2004/008609

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7	C07K1/22	C07K1/32	C07K14/47	C07K14/74	G01N33/569
	A61K38/00	A61K39/00			

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE Geneseq 'Online!'  29 January 2004 (2004-01-29), "Human  Protein P13284, SEQ ID NO 10787."  XP002305086  retrieved from EBI accession no.  GSN:ADD45354  Database accession no. ADD45354  abstract  &amp; WO 03/016475 A (BAYER AG ; D URSO  DONATELLA (DE); BEFORT KATIA (FR); GEN  HOSPITAL CORP)  27 February 2003 (2003-02-27)</p> <p>-----</p> <p style="text-align: center;">-/-</p>	17,18, 23,29

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

1 February 2005

Date of mailing of the international search report

21.02.05

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE Geneseq 'Online! 22 April 2004 (2004-04-22), "Human apoptosis-associated protein SEQ ID 154." XP002304913 retrieved from EBI accession no. GSN:ADI62711 Database accession no. ADI62711 abstract &amp; WO 03/058021 A (XANTOS BIOMEDICINE AG ; KESPER BJOERN (DE); SCHAEFER ROLF (DE); KAZINS) 17 July 2003 (2003-07-17) claim 48</p> <p>-----</p> <p>WO 93/18153 A1 (SMITH, GEOFFREY, LILLEY) 16 September 1993 (1993-09-16) page 9, line 28 - page 10, line 2; figures 2, cont. page 20, line 12 - line 17 -&amp; DATABASE EPO Proteins 'Online! 19 October 1999 (1999-10-19), "Sequence 25 from Patent WO9318153." XP002315336 retrieved from EBI accession no. EPOP:A76385 Database accession no. A76385 -&amp; DATABASE EPO Proteins 'Online! 19 October 1999 (1999-10-19), "Sequence 34 from Patent WO9318153." XP002315337 retrieved from EBI accession no. EPOP:A76394 Database accession no. A76394</p> <p>-----</p> <p>DATABASE Geneseq 'Online! 19 August 2002 (2002-08-19), "Human peptide encoded by genome-derived single exon probe SEQ ID 30218." XP002315338 retrieved from EBI accession no. GSN:ABG40553 Database accession no. ABG40553 the whole document &amp; WO 01/86003 A2 (MOLECULAR DYNAMICS, INC., USA) 15 November 2001 (2001-11-15)</p> <p>-----</p> <p>DI BARTOLO, V. ET AL: "Binding of human GM-CSF to synthetic peptides of the alpha subunit of its receptor" JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH , 16(1 &amp; 2), 77-92 CODEN: JRETE; ISSN: 1079-9893, 1996, XP009043176 page 79 - page 80; table 1 page 89 - page 90</p> <p>-----</p>	17,18, 23,28,29
X		1,10, 15-19
X		1,10, 15-19
X		1,12, 15-19

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International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CARR P D ET AL: "Structure of the complete extracellular domain of the common beta subunit of the human GM-CSF, IL-3, and IL-5 receptors reveals a novel dimer configuration."  <i>CELL</i>. 26 JAN 2001,  vol. 104, no. 2,  26 January 2001 (2001-01-26), pages  291-300, XP002315334  ISSN: 0092-8674  the whole document</p> <p>-----</p> <p>TSARK ELEANOR C ET AL: "Differential MHC class II-mediated presentation of rheumatoid arthritis autoantigens by human dendritic cells and macrophages."  <i>JOURNAL OF IMMUNOLOGY</i> (BALTIMORE, MD. : 1950) 1 DEC 2002,  vol. 169, no. 11,  1 December 2002 (2002-12-01), pages  6625-6633, XP002304908  ISSN: 0022-1767  cited in the application  the whole document</p> <p>-----</p> <p>SANTAMBROGIO L ET AL: "Extracellular antigen processing and presentation by immature dendritic cells"  <i>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA</i>, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US,  vol. 96, no. 26,  21 December 1999 (1999-12-21), pages  15056-15061, XP002222004  ISSN: 0027-8424</p> <p>-----</p> <p>FRIEDE T ET AL: "Natural ligand motifs of closely related HLA-DR4 molecules predict features of rheumatoid arthritis associated peptides."  <i>BIOCHIMICA ET BIOPHYSICA ACTA</i>. 7 JUN 1996,  vol. 1316, no. 2,  7 June 1996 (1996-06-07), pages 85-101,  XP002304909  ISSN: 0006-3002</p> <p>-----</p> <p>DONGRE A R ET AL: "In vivo MHC class II presentation of cytosolic proteins revealed by rapid automated tandem mass spectrometry and functional analyses."  <i>EUROPEAN JOURNAL OF IMMUNOLOGY</i>. MAY 2001,  vol. 31, no. 5, May 2001 (2001-05), pages  1485-1494, XP002304910  ISSN: 0014-2980  cited in the application</p> <p>-----</p>	12

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHICZ R M ET AL: "SPECIFICITY AND PROMISCUITY AMONG NATURALLY PROCESSED PEPTIDES BOUND TO HLA-DR ALLELES" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 178, no. 1, 1 July 1993 (1993-07-01), pages 27-47, XP002069888 ISSN: 0022-1007 cited in the application</p> <p>-----</p> <p>ARUNACHALAM B ET AL: "Intracellular formation and cell surface expression of a complex of an intact lysosomal protein and MHC class II molecules." JOURNAL OF IMMUNOLOGY (BALTIMORE, MD. : 1950) 15 JUN 1998, vol. 160, no. 12, 15 June 1998 (1998-06-15), pages 5797-5806, XP002304911 ISSN: 0022-1767</p> <p>-----</p> <p>DATABASE UniProt 'Online! 1 November 1996 (1996-11-01), "Cytokine receptor complex common beta chain h beta c (Fragment)." XP002315339 retrieved from EBI accession no. UNIPROT:Q63968 Database accession no. Q63968</p> <p>-----</p> <p>CANTAGREL A ET AL: "Interleukin-1beta, interleukin-1 receptor antagonist, interleukin-4, and interleukin-10 gene polymorphisms: relationship to occurrence and severity of rheumatoid arthritis." ARTHRITIS AND RHEUMATISM. JUN 1999, vol. 42, no. 6, June 1999 (1999-06), pages 1093-1100, XP002315335 ISSN: 0004-3591</p> <p>-----</p> <p>RAMMENSEE H-G ET AL: "MHC LIGANDS AND PEPTIDE MOTIFS: FIRST LISTING" IMMUNOGENETICS, SPRINGER VERLAG, BERLIN, DE, vol. 41, no. 4, February 1995 (1995-02), pages 178-228, XP000673045 ISSN: 0093-7711</p> <p>-----</p>	

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

2,10,12 (complete), 1, 14-19, 23-28, 29 (partially)

4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 2 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from Interferon-gamma-inducible lysosomal thiol reductase (GILT, SEQ ID NOs: 1-3, 49); use of GILT as a marker for rheumatoid arthritis (SEQ ID NO: 40)

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Invention 2: claims 3 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from Integrin beta-2 (SEQ ID NOs: 58, 59, 103); use of integrin beta-2 as a marker for rheumatoid arthritis (SEQ ID NO: 123)

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Inventions 3-29: claims 4-13, 27 (complete), 1, 14-19, 23-26, 28, 29 (all partially)

MHC class II antigenic peptides derived from phosphatidylinositol-4,5-bisphosphate 3-kinase (SEQ ID NO: 60, 104), urokinase-type plasminogen activator (SEQ ID NO: 61, 105), immunoglobulin heavy chain V-III region (SEQ ID NO: 62, 106), DJ-1 protein (SEQ ID NO: 63, 107), apolipoprotein B-100 (SEQ ID NO: 4, 5, 50), 26S proteasome non-ATPase regulatory subunit 8 (SEQ ID NO: 64, 108), Interleukin-1 receptor (SEQ ID NO: 68, 109), fibromodulin (SEQ ID NO: 69, 70, 110), GM-CSF/IL-3/IL-5 receptor (SEQ ID NO: 71, 72, 111), sorting nexin 3 (SEQ ID NO: 73, 112), inter-alpha-trypsin inhibitor heavy chain H4 (SEQ ID NO: 6-12, 51), complement C4 (SEQ ID NO: 13-18, 52), complement C3 alpha chain (SEQ ID NO: 19-23, 74, 75, 53), complement C3 beta chain (SEQ ID NO: 76, 77, 113), SH3 domain-binding glutamic acid-rich-like protein 3 (SEQ ID NO: 24-27, 54), interleukin-4 induced protein 1 (SEQ ID NO: 28-30, 55), hemopexin (SEQ ID NO: 31-35, 78, 56), Hsc70-interacting protein (SEQ ID NO: 36-39, 57), invariant chain (Ii) (SEQ ID NO: 79-83, 114), retinoic acid receptor responder protein 2 (SEQ ID NO: 84-86, 115), fibronectin (SEQ ID NO: 87-91, 116), cathepsin B (SEQ ID NO: 92, 117), tripeptidyl-peptidase II (SEQ ID NO: 93, 94, 118), legumain (SEQ ID NO: 95, 119), platelet activating factor receptor (SEQ ID NO: 96, 120), poly-alpha-2,8-sialyltransferase (SEQ ID NO: 97, 121), ras-related protein Rab-11B (SEQ ID NO: 98-102, 122); use of said polypeptides as markers for rheumatoid arthritis (SEQ ID NO: 41-48, 124-141)

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Invention 30: claims 20-22

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

method for isolating and identifying MHC class II associated  
RA antigenic peptides

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**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No	
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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
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**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

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WO 0186003	A2	WO 0157276 A2	09-08-2001